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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/070,295

09/09/2002

Menachem Rubinstein

RUBINSTEIN=7

2828

1444 7590 01/30/2009
BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER

CHANDRA, GYAN

ART UNIT

PAPER NUMBER

1646

MAIL DATE

DELIVERY MODE

01/30/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/070,295

Applicant(s)

RUBINSTEIN ET AL.

Examiner

GYAN CHANDRA

Art Unit

1646

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 January 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 5,9,11,12,15-17 and 19 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 5,9,11,12,15-17 and 19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/S506)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Applicant's response filed on 1/07/2009 is acknowledged and fully considered.

Status of Application, Amendments, And/Or Claims

Claims 5, 9, 11, 12, 15-17 and 19 are pending and examination on the merit to the extent that they read on the elected invention of VEGF inhibitor – CSC.

Response to Arguments

Claim Rejections-maintained

Claim Rejections - 35 USC § 112-enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5, 9, 11, 12, 15-17 and 19 stand rejected under 35 U.S.C. 112, first paragraph-enablement for the reasons of record in pg. 5-10 of the Office Action of 2/13/2006, in pg. 3-5 of the Office Action of 4/5/2007, and in pg. 3-6 of the Office Action of 10/7/2008.

The instant claims are drawn to a method for inhibiting angiogenesis in adipose tissues in mammals comprising administering to a subject a pharmaceutical composition comprising (i) leptin, (ii) a leptin fragment, (iii) a leptin homolog having 90% sequence identity with sequence of leptin, or (iv) a derivative of leptin or leptin homolog which has the activity of leptin, and optionally, an inhibitor of angiogenesis in a suitable dosage, (v) wherein angiogenesis inhibitor is a VEGF inhibitor, (vi) wherein the

derivative said derivative has one or more chemical moieties attached to leptin, (vii) wherein said chemical moieties are water soluble polymers, wherein said polymers are polyethylene glycol, and wherein VEGF is absent in the adipose tissue.

Applicants argue (pages 3-9 of Response of 1/07/2009) that (i) the similar to the rat corneal model the knockout model is another well accepted model for studying the effect of one given molecule/protein; (ii) leptin is angiogenesis inducer only in rat corneal cells, human umbilical vein endothelial cells (HUVECs) and porcine aortic endothelial cells (PAECs) but not in adipose tissue as the art does not specifically teach the effect of leptin on adipose tissues, and (iii) the references Holmes et al and Teichert-Kuliszewska et al do not teach angiogenesis in adipose tissues.

Applicants' arguments have been fully considered but they are not persuasive because the instant rejection is under 35 U.S.C. 112, first paragraph- enablement the specification only teaches that leptin inhibits angiogenesis in -ob/-ob mouse or adipose tissue in ob/- mouse. The disclosure does not provide any support that the administration of leptin in any normal mammal inhibits angiogenesis in adipose tissue. Applicants' arguments that similar to the well accepted rat corneal model, the knockout model of the instant invention is also suitable for studying angiogenesis have been fully considered but they are not persuasive because the ob/- mice are art well accepted model for obesity, but not for angiogenesis. The art has established that the administration of leptin promotes wound healing which requires angiogenesis (previously presented, Frank et al, J. Clin. Invest. 106: 501-509, 2000; Sierra-

Honigmann (U.S. Pub. No. 2007/0275874 A1) and that leptin promotes angiogenesis in pre-adipocyte of normal mammal (previously presented, Park et al), one skill in the art would not conclude the role of leptin as an angiogenic inhibitor in adipose tissue of normal mammals, unless evidence to contrary. Applicants' arguments that the references Holmes and Teichert-Kuliszewska do not teach that leptin inhibits angiogenesis in adipose tissue of a mammal have been fully considered but they are persuasive in part that the references do not measure angiogenesis in adipose tissue of a normal mammal, but because the disclosure is devoid of any guidance or example from a normal mammal to support that leptin inhibits angiogenesis in adipose tissue one of the skill in the art would not know that leptin inhibits angiogenesis in adipose tissue of a normal mammal. Since the specification discloses that the administration of leptin in ob-/- mice inhibits angiogenesis in adipose tissue, the Examiner indicates that the claims drawn a method of inhibiting angiogenesis in ob-/- mice by administering leptin are allowable.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GYAN CHANDRA whose telephone number is (571)272-2922. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gyan Chandra
Art Unit 1646
22 January 2009
Fax: 571-273-2922

/Robert Landsman/
Primary Examiner, Art Unit 1647